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(54) Title: **REPLICATION COMPETENT HEPATITIS C VIRUS AND METHODS OF USE**

(57) Abstract: The present invention provides replication competent polynucleotides that include a coding sequence encoding a hepatitis C virus polyprotein having adaptive mutations. The invention also includes methods for making replication competent polynucleotides, identifying a compound that inhibits replication of a replication competent polynucleotide, selecting a replication competent polynucleotide, and detecting a replication competent polynucleotide.